

WHAT IS CLAIMED IS:

1. A process for the preparation of a procyanidin dimer, which process comprises the steps of:

(a) protecting each phenolic hydroxyl group of a procyanidin monomer with a removable protecting group which does not deactivate the A ring of the monomer, wherein the protecting step is carried out in an aprotic solvent;

(b) activating for coupling the C-4 position of the compound of step (a) by introducing an acyloxy group using a lead (IV) salt of an organic acid to provide an activated compound; and

(c) coupling the activated compound of step (b) with an unprotected procyanidin monomer in the presence of a coupling catalyst to produce the dimer.

2. A process for preparing a linear procyanidin oligomer, which process comprises the steps of:

(a) preparing a partially protected procyanidin dimer, wherein the phenolic hydroxyl groups of the top mer are protected with a removable protecting group which does not deactivate the A ring of the protected mer;

(b) masking the unprotected phenolic hydroxyl groups of the bottom mer of step (a) and the hydroxyl groups at both C-3 positions with a removable masking group which deactivates the bottom mer of said masked, protected dimer;

(c) deprotecting the top mer of the dimer of step (b) to provide a deprotected masked dimer thus allowing coupling to occur at the C-8 position of the deprotected top mer of the dimer;

(d) coupling the dimer of step (c) with an unblocked or blocked, protected, activated monomer to form a trimer, wherein the top mer of the trimer is a protected blocked mer or a protected unblocked mer and is coupled at the C-8 position;

(e) masking the blocked or unblocked trimer of step (d);

(f) deprotecting the blocked or unblocked, protected, masked trimer of step (e) to form an blocked or unblocked trimer;

and

(g) optionally repeating or alternating steps (a) to (f) to prepare higher oligomers wherein the number of mers are 4 to 18.

3. A process for preparing a branched procyanidin oligomer, which process comprises the steps of:

(a) preparing an unblocked or blocked, partially protected procyanidin dimer, wherein the phenolic hydroxyl groups of the top mer are protected with a removable protecting group which does not deactivate the A ring of the protected mer and while the bottom mer has free phenolic hydroxyl groups;

(b) coupling the dimer of step (a) with a unblocked or blocked, protected, activated procyanidin monomer to form a branched trimer;

(c) deprotecting the trimer of step (b); and

(d) optionally carrying out one of the following steps in a sequential, alternating or combinational fashion to provide procyanidin oligomers having 4 to 18 mers comprising (4→8), (4→6) (6→4), and/or (8→4) linkages;

(i) coupling the trimer of step (c) with an unblocked or blocked protected procyanidin monomer; or

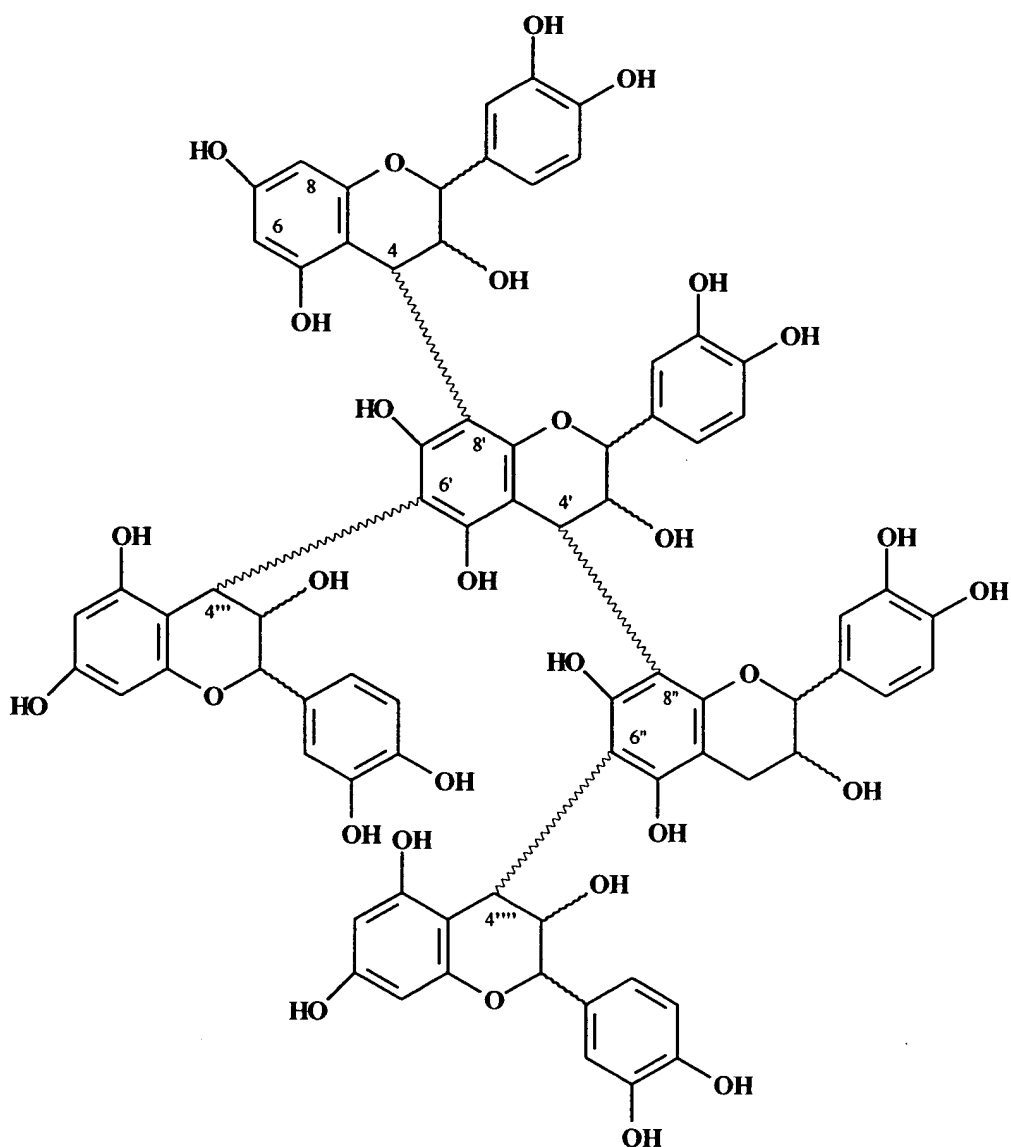
(ii) masking the trimer of step (b); deprotecting the masked trimer; and coupling the masked trimer with an unprotected or protected, blocked activated procyanidin monomer.

4. A process for obtaining the procyanidin dimer of Claim 1, linear procyanidin oligomer of Claim 2, or branched procyanidin of Claim 3, which further comprises the step of deprotecting the dimer or oligomer and, if necessary, demasking and/or deblocking the dimer or the oligomer.

5. The process of Claims 2 or 3, wherein n is 5-12.

6. The process of Claim 5, wherein n is 5.

7. The process of Claims 1, 2, or 3, wherein the epicatechin or catechin monomers are the same or different.
8. The process of Claim 2, wherein the linkages are (4→6) or (4→8).
9. The process of Claim 3, wherein the linkages are (4→6), (4→8), (6→4) and/or (8→4).
10. The process of Claims 2 or 3, wherein the demasking step is carried out by base hydrolysis.
11. The process of Claims 1, 2, or 3, wherein, in the protecting step, the protecting group is benzyl, *p*-methoxybenzyl, *t*-butyl, or trityl and wherein the aprotic solvent is dimethyl formamide, dimethylacetamide, or dimethyl sulfoxide.
12. The process of Claims 1, 2, or 3, wherein the activating group is acetoxy, formyloxy, or propionyloxy; wherein the lead salt is lead tetraacetate, lead tetraformate, or lead tetrapropionate; and wherein the solvent is benzene.
13. The process of Claims 12, wherein the activating step is carried out using an organic acid.
14. The process of Claim 13, wherein the organic acid is the same as that used for the lead salt.
15. The process of Claim 14, wherein the organic acid is formic acid, acetic acid, or propionic acid.
16. The process of Claim 2 or 3, wherein the blocking group is a halo group.
17. The process of Claim 16, wherein the halo group is a bromo or an iodo group.
18. The process of Claim 2 or 3, wherein the deblocking step is carried out with an alkyl lithium.
19. The process of Claim 18, wherein the alkyl lithium is *n*-butyl lithium or *tert*-butyl lithium.
20. The process of Claims 1, 2, or 3, wherein the deprotecting step is carried out by hydrogenolysis.
21. A doubly branched oligomer having the structure:



22. A process for preparing the doubly branched oligomer of Claim 21, which comprises the steps of:

(a) protecting each phenolic hydroxyl group of a first procyanidin monomer with a first protecting group which does not deactivate the A ring of the monomer, wherein the protecting step is carried out in an aprotic solvent to provide a protected monomer;

(b) activating for coupling the C-4 position of the compound of step (a) by introducing an acyloxy group using a lead salt of an organic acid to provide an activated, protected monomer;

(c) coupling the monomer of step (b) with an unprotected procyanidin monomer in the presence of a coupling catalyst to provide a partially protected dimer;

(d) acetylating the dimer of step (c) to provide an acetylated, partially protected dimer;

(e) deprotecting the acetylated partially protected dimer of step (d) to provide an acetylated dimer;

(f) coupling the acetylated dimer of step (e) with a 4 β -acetoxy protected monomer to produce a trimer;

(g) deacetylating the trimer of step (f);

(h) coupling the trimer of step (g) with a 4 β -acetoxy monomer to produce the doubly linked procyanidin pentamer; and

(i) deacetylating and deprotecting the doubly linked procyanidin pentamer of step (h) to produce the deprotected doubly branched procyanidin tetramer.

23. The process of Claim 22, further comprising repeating steps (a) to (c) to produce a multiply branched procyanidin oligomer comprising n monomers, wherein n is an integer from 6 to 18.

24. A process for producing a procyanidin dimer having a (8 \leftrightarrow 8) linkage, said process comprising the steps:

(a) reacting a first 8-bromo protected monomer with a hexaalkyl distannane in the presence of palladium_(o) to provide a protected monomer-8-trialkyl stannane;

(b) coupling the product of step (a) with a second 8-bromo protected monomer with tetrakis (triphenyl phosphine) palladium_(o) in benzene to produce a (8 \leftrightarrow 8) coupled dimer; and

(c) deprotecting the product of step (b) to produce the (8 \leftrightarrow 8) dimer.

25. A process for producing a procyanidin dimer having a (6 \leftrightarrow 6) linkage, said process comprising the steps:

(a) reacting a first 6-bromo protected monomer with a hexaalkyl distannane in the presence of palladium_(o) to provide a protected monomer-6-trialkyl stannane;

(b) coupling the product of step (a) with a second 6-bromo protected monomer with tetrakis (triphenyl phosphine) palladium_(o) in benzene to produce a (6↔6) coupled dimer; and

(c) deprotecting the product of step (b) to produce the (6↔6) dimer.

26. A process for producing a procyanidin dimer having a (6↔8) linkage, said process comprising the steps of:

(a) reacting a first 6-bromo protected monomer with hexaalkyl distannane in the presence of palladium_(o) to provide a protected monomer-6-trialkyl stannane;

(b) coupling the product of step (a) with a second 8-bromo protected monomer with tetrakis (triphenyl phosphine) palladium_(o) in benzene to produce a (6↔8) coupled dimer; and

(c) deprotecting the product of step (b) to produce the (6↔8) dimer.

27. A process for producing a procyanidin dimer having a (8↔6) linkage, said process comprising the steps:

(a) reacting a first 8-bromo protected monomer with a lithium trialkyl tin to provide a protected monomer-8-trialkyl stannane in the presence of palladium_(o);

(b) coupling the product of step (a) with a second 6-bromo protected monomer with tetrakis (triphenyl phosphine) palladium_(o) in benzene to produce a (8↔6) coupled dimer; and

(c) deprotecting the product of step (b) to produce the (8↔6) dimer.

28. A crystalline 8-bromo-tetra-*O*-benzyl (-) epicatechin.